

Banishing loneliness with a 1000 year functional depot injection or possibly as a combined effect with another drug could cause 26% less mortality, ““Imagine a condition that makes a person irritable, depressed and self-centred, and is associated with a 26 per cent increase in the risk of premature mortality,” Cacioppo and her late husband, John Cacioppo, wrote in The Lancet last year. Around a third of people in industrialized countries report feeling lonely, one in 12 severely so”

<https://nationalpost.com/health/all-the-lonely-people> Notably the steroidal hormone pregnenolone has been researched as an anti-loneliness drug, and as a sex steroid like molecule could have ethynylation as well as halogenation as effective dose multipliers; the first page of a search

engine suggests 10 times greater effect per dose, if ethynylation is 8 times greater dose efficacy then 80 times fewer micrograms per dose could be possible; at .625 mg as a daily estrogen dose, and 300-800 nanogram/24 hours at ethynylized estrogens or possibly progestones (progestins), the fluorinated version could be active at 30-80 nanograms/24 hours, or a .333 gram depot injection providing 365,000 to one million gradually diffused 1 microgram to 100 nanogram doses at a one office visit dose treatment for loneliness, a 1000 to 10,000 year duration of loneliness reduction if pregnenolone has a ethynyl and fluoro dose amplified form. If a lymphatic system applied depot form of ethynylated halogenated progesterone is possible that approximately quadruples

physiological availability from omitting first pass metabolism; if a blood brain barrier passing moiety is a possible modification as well a two to ten times greater availability at the CNS, a possible location of feelings of loneliness could be possible, so 80 nanograms /4 /2 is 10 nanograms per 24 hour dose, permitting an approximately 40 milligram 1000 year duration depot injection dose.

Notably, if it is possible to make an oral depot version of a drug, possibly from antibodies linked to palmitates, with the antibodies specific to lymphatic epithelia, then at 10% efficiency compared with an injected depot a 400 mg depot producing oral dose with 1000 year depot functionality of a ethynyl fluoropregnenolone could be possible; gene therapy or also germline gene therapy to produce more

pregnenolone, or shift to personality genetics that is absent feelings of loneliness; also noting that the big five personality test trait areas are about 50% heritable, and that a new personality test where, like the minnesota multiphasic personality inventory the questions were correlated, winnowed, and enhanced to be predictive, it is possible a 97-99% genetically predictable paper question or also software psychology test with completely fresh new traits that could also be called themes could be constructed. If some percentage of these traits or themes that are 97-99% genetically predictable are the kinds of things people would change to improve their well being, efficacy, ability, and prosociality, reduce or prevent loneliness, while maintaining or expanding creativity and initiative then those are rapidly eugenics

addressable traits and themes that could also be gene therapy opportunities.

Addressing loneliness with depot drugs or causing greater plasma levels from less pregnenolone metabolism, whichever is more physiologically beneficial could reduce mortality 26%. It is unknown if numerous species of mammals along with humans experience loneliness, gene drive could banish loneliness at perhaps all mammals; the effect on frequency of mating and the number of progeny is unknown, but imaginably increases among all mammals that experience an absence of loneliness.

Moieties that cause higher physiological availability and physiological activity at a particular

mg (or mcg or ng) dose; I read that halogenated drugs are less metabolized at the liver with things like CYP enzymes, that gives longer plasma duration, as well as possibly omits first pass metabolism, causing, imaginably, 90% or higher amounts of the drug to remain functional at the circulatory system; It could be that there is a kind of drug visiting and detaching from receptors many times, as well as what I previously thought that halogenated drugs glom on to receptors and have long residence intervals from their high electronegativity glomming and staying on a receptor; also it is possible that halogenated drugs, as well as other drugs, which get some of their durability from plasma from glomming to albumins, globulins, or other plasma proteins could have versions that glom to plasma proteins

twice as avidly, or perhaps are absent any plasma protein glomming; a fluorodrug without plasma protein glomming might go almost completely unmetabolized at the liver, yet have a tissue available dose 7-9 times higher from an oral or other dosing; alternately, double duration plasma protein glomming

screen a library: radiolabelled or fluorophore labelled halogenated drugs, a few thousand, million, billion, or at a 300mm integrated circuit wafer with 1 trillion wells

Rapamycin, with like a trifluoro (methyl group like with three fluorines) that has 16 day or longer plasma half life, different plasma protein glomming could be an even more effective enhanced human longevity drug, from persisting at the

circulatory system longer; noting the mice that lived 60% longer from 126 ppm rapamycin had frequent meals but, I perceive I may have read, 9 minute rapamycin plasma half life, and I might have read human plasma half life of rapamycin might be .9 hours while wikipedia says 57-63 hours; higher plasma protein glomming of a rapamycin; wikipedia says rapamycin is 92% protein glommed, there is some possible greater sustained rapamycin longevity effect there that could be produced and be beneficial; wikipedia says, “Since albumin is alkalotic, acidic and neutral drugs will primarily bind to albumin.”; Although a trained professional would know much more, the longest plasma half life of a drug I am aware of is norfluoxetine, 16 days, 384 hours; perhaps the chemistry of such drugs (trifluoride like a methyl)

could be used to produce even more beneficial, possibly even more longevizing variations of rapamycin, noting the mice were likely eating food perhaps every few minutes at the 126 ppm enteric coated rapamycin dose; At the rapamycin molecule I read that a $\text{C}(\text{CH}_3)_3$ with numerous $\text{C}(\text{CH}_3)_2$ is thought to be the mTOR active part of rapamycin, and it has a methyl on it that if replaced with a trifluoro methyl like moiety could cause the ten times greater plasma half life. It is different than other things I have read, but wikipedia says ascorbic acid has a circulatory system half life of 83 days, with an elimination constant of 4 months, that suggests something as simple as screening a variety of locations of an ascorbic acid moiety could make a 3 month dose of a longevity producing rapamycin variant; also I perceive I

read that rapamycin's oral absorption has to do with rapamycin's nonsensitivity to pH, a rapamycin ascorbic acid version could have higher effective drug absorption at a particular mg or ppm at food dose;

Longevity drug: 126 ppm rapamycin is published as making mice live 60% longer, it is my perception that I read this has to do with reducing mTOR activity, notably though mice with mTOR $-/-$ genes, which I perceive as meaning they have zero mTOR receptors live 20% longer; It seems possible that at mammals with mTOR receptors the mammals might also be making previously unstudied slightly hormesis-like chemicals that cause other changes at the body to compensate or ameliorate for having mTOR receptors, and possibly reducing the activity of things

(networks) connected to mTOR receptor activation; those slightly hormetic like ameliorators persist at the mammals when rapamycin causes the 60% greater mouse lifespan yet at the -/- mtor mice are minimally there (genes that produce the ameliorating chemicals) as they do not need to be. Finding those physiochemicals, likely proteins, receptor proteins or material at the cytoplasm then administering them to mammals as separate longevity chemicals as drugs could have the 40% longevity increase that could be linked to 60% increased longevity mice (minus) 20% at mice with no mTOR receptors; At humans, production of these chemicals, proteins, or peptides could be endogenous with germline gene modification or also gene therapy; The possibly attainable 40% greater longevity from other mTOR receptor

presence ameliorators might even have different tissue or cyte localizations, potentially concentrating longevizing effects, or finding areas to bring up to the body tissue longevity increasing median, which would cause greater youthfulness of phenotype as well as greater longevity; looking at all the mRNA that rapamycin causes the production of, and comparing it to the mRNA that the mTOR $-/-$ mice when administered rapamycin make could find the ameliorator 40% greater longevity genes and chemicals, just administering rapamycin to the mTOR $-/-$ mice could find the 40% longevity mTOR ameliorating chemicals, genes, and proteins or peptides from mass characterizations at all the proteins and peptides produced at the mammals.

Moving a math distribution of

longevizing drug effects with bulk-effect different longevity drugs, and comparing that to a concatenated tissue and cyte approach; is there published research on the distribution of phenotypic and genotypic youthification of form (variously somatic form or things like telomeres or mRNA expression profiles) at different cytes and tissues, It is possible an equation, computer model, or predictive AI would be much better, although one way to think of this is like a histogram; if the histogram has a normal distribution then 32% of tissues and cytes are high longevity responders, 68% are at the first standard deviation; broad-group differences in distribution shape, and addressing which cytes and tissues are at what standard deviation could be a programmatic way to find composite longevity drug

combinations that cause a chemical that causes the phenotypic or also genotypic central standard deviation of one drug to be at the 2nd standard deviation of longevization with another drug; this bulk mathematical effect complements the other idea of finding things like: one thing functions at adipose tissue, one thing works at neurons, another thing works at the cardiovascular system, another works on preventing cancer then assembling a multitissue multicyte addressing multidrug blend; both have value, it is just that addressing entire distributions to move up an entire standard deviation of longevity increase could be accomplished with particularly larger affordability, and simplicity.

Numerous math approaches, or groups of drugs/activities/genetic

enhancements could be numerically modelled or equation limited to find the component groups that most functionally cause longevizing distribution standard deviation shifts, overlays, and complementary groups; Receptor based, like AMPK and less mTOR, IGF-1, and possibly receptors activated from published as causing 25-27% greater mouse longevity royal jelly chemicals or proteins, could be a standard deviation described group; then a completely different chemical group of nonreceptor longevity increasing drugs could be another distribution group, like senolytics; a third group could be what I read about that might be called “mortality reducers” epithalon combined with thymosin causes four times fewer people to have mortality events after six years, preventing, curing, or also genetically precluding loneliness

reduces mortality 26%, I perceive there are other mortality reducers; another producible group that could actually cause standard deviation overlap and movement of more things to second deviation or higher of greater longevity effects is to just make lipophilic and hydrophilic variations on the most effective longevity drugs; a hydrophilic and lipophilic version of the rapamycin molecule and other receptor molecules, a lipophilic and hydrophilic version of senolytics, a lipophilic and hydrophilic version of 17 alpha estradiol, a lipophilic and hydrophilic version of the 25-27% greater longevity royal jelly proteins or other chemicals; Also possibly lipophilic and hydrophilic and lymphatic system versions of what might be non-receptor longevity drugs like spermidine, immunizations, and NMN,

could each modify the distributional histogram of effectiveness, which might be a normal distribution at any one group of longevity drugs that could combine to move as many tissues and cytes as possible to produce an almost three-phase power like graph with all three phases being at the second deviation (upper 32%) of higher of longevity effect.

A three of four drug blend that shifts entire distributions could have, perhaps based on the math of drug combination alone, many fewer numerically predictable side effects or contraindications than a 400 tissue or 400 cell type multihundred drug composite. Then again, if each of the 400 drugs or gene products individually causes greater longevity and wellness, then their harmlessness might be kind of definitionally

adequate, sort of, if it makes you live longer, and makes you weller, its harmlessness is definitionally adequate. Note though that testing and time to commercialization could be much quicker with 10 highest effect longevity drugs times 6 variations (lipophilic, hydrophilic, halogenated and ethynylized, depot form, lymphatic area, gene based,) than testing and time to commercialization of a multihundred drug form. Notably though there are numerous opportunities for tremendous benefit from individual drugs as well, gene therapy or also germline modification to produce longevity and mortality reducing peptides (epithalon with thymosin 4 times mortality reduction)

Mass screening of longevity drug candidates with vertebrates: Fish:

some fish (a goby) have median lifespans of 60 days, others like guppies, 2 years; A fish listed online is .55 inch (1.4 cm), Danionella, “When the genus was first described, these fish were classified as the smallest adult vertebrates to inhabit freshwater”; Other fish in the .75 inch to 1 inch size are described at <https://www.myaquariumclub.com/nano-fish-for-small-aquariums-5134.html>; **Some fish may have greater cognitive ability than some other fish**, “Dwarf puffers are one of the few species of fish that interact with their environment and owner. They will happily greet you as you approach the tank, and can even learn to be hand fed.”; another consideration for mass screening of longevity molecules and longevity genetics and wellness molecules and wellness genetics at vertebrates is absence of aggression;

it is possible that at a communal growth tank frequent fish-fish interaction of a nonpleasant nature could affect physiology, actual physical integrity, and even the effects of stress on longevity;

Mass screening the fish: at 1 second per fish, a 3d printed 100 fish hydrosorter processes 1 million vertebrate fish for longevity drug efficacy at 10,000 seconds or 167 minutes (2.8 hours); A different engineering version: noting tube lengths, even with green light causing many fish to prefer forward travel, at 10 seconds per fish, and a 1000 fish (32 times 32 grid) hydrosorter process it is also 2.8 hours to characterize and label 1 million fish; 117 days screens 1 billion fish.

The hydrosorter could be 3d printed

so a fresh, absent algae coating, predictable fluid flow hydrosorter is available anytime. One Kg of 3d printing filament is \$29; If the hydrosorter has a mass of 1 Kg or likely much less, then a 3d printed version is \$29 That makes CAD development of greater and greater efficacy hydrosorters more rapid, and causes the most complex part to be \$29, disposable, and like PLA (polylactic acid), physiologically compatible and harmless.

At the growth tank, fish can be taught light stimulated fish behaviors, green could mean swim towards something, possibly a food source that will dispense food in 2-7 seconds; Blue light could teach the fish to be stationary in the water, possibly facilitating imaging, Aqua light could be linked to the learning of a 3-7

sequence action the fish could perform for the cameras at the hydrosorter, providing data on cognitive effects at progressive living, White light could teach fish to expect change without stress; perhaps a mini version of the hydrosorter at the growth tank, only without the cameras, lasers, and other imagers;

Cognitive or cognitive like-distribution shifts, could be measured at the hydrosorter, with accuracy of the aqua light learned sequence, and with efficacious cameras and software, inter-motion time, kind of like velocity of recall; To keep fish moving through the 1000 channel hydrosorter there could be green light stimulated fish preference for forward travel,

To label individual fish for further study, GFP or another photoshiftable

color, then a laser, absent effect on actual fish tissue, barcodes the fish with photochemical modification of just the GFP at 1 million fish labelled each 2.8 hours, also, all the fish that go through the hydrosorter, notably the labelled fish, can be reused from the after hydrosorter tank, to multiplex treatments; Also, fish the software notes to be of particular interest, like the youngest phenotype fish out of each million, or if the fish seem euphoric, unusually physically active, or displays mating behaviors at the camera area of the hydrosorter then those effects, potentially beneficial at mammals, can be linked to the longevity chemicals and genes being screened;

There are numerous ways to administer longevity drugs to fish, the hydrosorter could dispense a couple

drugged food pellets at a particular area of the hydrosorter, where the mechanism at the hydrosorter could utilize something like $n=40$ for each different longevity drug, to administer 25,000 different longevity drugs in 2.8 hours, if the fish get 3 hydrosorter administered doses, separated at 24 hours each, then a full hydrosorter imaging, that is 11.2 hours spread over 96 hours at an automatic system; I once had a motorized automatic fishfeeder that was about \$29.99; Another possible way to administer drugs to fish is to have something like an inkjet printer spray them with a gelcoat, another way is to have the hydrosorter have the fish breathe drugged water through their gills for a minute at one area of the hydrosorter;

Fish vertebrate research supporting well and longevized human babies:

one benefit of using vertebrates like fish as longevity drug development and effectiveness verifiers is that some fish are livebearers of young, this provides an opportunity to see if there are any beneficial new drug distribution shifting effects of well progeny; it is possible some longevity drugs as well as genes actually heighten fetal and baby wellness, scanning a million fish in 2.8 hours is one way to find drugs that can then be tested on mammals like mice to find out if fetal and baby well being are increased at mammals as well.

The hydrosorter could be a little like the top view of the internal crenellations of cardboard at about 14 mm width, with sensors tht can see through the 3d printed polymer or a transparent plastic plate on top of the

hydrosorter, so one or more cameras can image the 1000 simultaneous fish for software processing; Notably things like THz imaging of the fish could work through the 3d printed polymer and the software could record things like organ size and skeletal density, and gill respiration rate, and heartrate, Also, light cameras placed at CAD optimized ports at the 3d printed hydrosorter are also possible, and general soft illumination provided through the 3D printed volume with external lighting;

With positron emission tomography and radiolabelled physiochemicals like like radiolabelled longevity drugs that effect neurons, radiolabelled neurotransmitters, other tissues and molecules, as well as concentration and multiple measurements with time activity at the physiological tissues

with the least vascularization, Then variations or shifts from the longevity drug molecule compared with untreated fish' distribution of tissue activities and neural function can be gathered as data at a computer and mapped; it is also possible that noting the 25,000 groups of $n=40$ fish (1 million) screened each 2.8 hours, that a variety of longevity drug localization effects will be found, and finding out which chemical concentrates where has longevizing and wellness value.

One use of the unique fish ID produced at something like a laser on GFP is the production of a library of frozen fish, possibly with detectable mRNA activity or things having other technology and drug development value, live clonability from the frozen fish, also detailed study of the 20-100 most efficacious longevity drugs' per

million fish characterized effect on things like cytoplasm, reproductive anatomy (sperm, eggs, livebearer growth areas), brain morphology, telomere length, cardiovascular fitness, cancer amount, and immune system effects;

One area of longevity molecule research doable at fish at a hydrosorter, is the longevizing effects of reducing the amounts of some molecules from tissues or at circulation; It is possible the hydrosorter could be used to administer gill-breathable antigens (immunizations) against things like interleukins, sex hormones that are absent effects on secondary sex characteristics yet have cardiovascular risks or carcinogenic effects, liver enzyme saturating endogenous chemicals, mTOR

activators, IGF-1 (and similar molecules), endogenous telomere length reducing molecules, endogenous AMPK activity decreasing chemicals, possibly some versions of cortisol-like molecules circulating endogenously, physiochemicals that get upregulated when organisms miss sleep and could be deleterious (missing one night of sleep doubles likelihood of infection at a human); peptides (or proteins) that cause stress, possibly like deleterious versions of beneficial peptides (or proteins) that occupy beneficial receptors, but have zero or negative activity, keeping the beneficial forms of those peptides (or proteins) from reaching the receptors and providing benefit, various lipopolysaccharides that might reach the circulatory system from the GI tract, histamine, the physiological chemicals produced

at gum disease that I read is like 20 something to 48% active at causing cardiovascular disease, Any endogenous physiochemicals that cause heart rhythms outside the wellness standard (although these are of course fish), as well as, noting that a combination of epithalon with thymosin causes four times less mortality during six years at humans, any chemicals that occupy epithalon and thymosin receptors causing those receptors to not function at preserving living function.

A peltier enabled hydrosorter used at fish could also be used to develop cryogenic cryoprotectants to support human cryonic preservation and revival.

Eugenics: The 3D printed hydrosorter could also be used to research a

variety, notably a screenable library of 100,000 or a million freeze dried sperm preservatives to find those that produce motile egg-seeking sperm on rehydration, a technology that benefits eugenics, and can cause the manufacturing cents of a sperm emitting vaginal decal or also paper applicator vaginal canal 60 day attaching paint that continually emits genetically enhanced or also genetically optimized sperm to be about 11 cents a month, or 1.21 annually. Notably, 25,000 different drugs and preservatives can be screened on 40 sperm each 2.8 hours. Screening a billion freeze dried sperm revival with motility molecules, concentrations, and chemical treatment sequences is less than 120 days. Another technological from is a \$4.14 5 gram polymer near cervix circlet that would gradually release 11

mg of motile previously freeze dried sperm every 24 hours for over a year, causing the likelihood of conception to be at 99% during the first 14.2 months of use among those persons capable of becoming pregnant

Gene therapy and gene drive on fish: At fish in the wild it might be notably effective to gather wild fish in multiplenum nets, where the netting is coated with gene transfection gel, and then the fish released after a 1-14 minute interval of gene transfer to transfect what might be millions of fish with gene drive every 24 hours, with 100 days from one boat causing 100-200 million gene drive enabled fish to communicate gene drive to other fish in the ocean, providing benefits to fish like removing all nociception as well as decreasing nipping and fish social behaviors

humans find ethically beneficial to obviate.

Beauty genes that decrease risk of cancer: It is possible that female sex hormone receptors like estrogen receptors have a genetic 100 to 700% different amount of responsiveness to the same amount of circulating estrogen, progesterones, or other sex hormones, that the size and shape and optimizability of human female secondary sexual characteristics like breast size and shape and soft skin and even body form (like I have heard of banana shape and top heavy hourglass) could be enhanced with human germline genetic enhancement of estrogen receptor responsiveness to be at the 700% range, notably actual circulating estrogen could be the 2019 median amount or possibly shifted to endogenous estrogenic,

progesteronic, or other sex hormone chemicals with just 10-50% of the cancer risk of 2019 AD median estrogen amounts or also particular estrogen molecule types, so this gives women and girls even more beautiful body form while reducing cancer risk 50-90%.

There is a possibility that a technology that immunizes against background endogenous amounts of the chemicals produced when a human misses sleep reduces developing infectious disease, precluding, like with immunization, these chemicals, that are around even when a person gets a normal amount of sleep, could reduce the incidence of many, or most infectious disease; I perceive I read that missing a night of sleep doubles risk of infection, it is possible that is from the production of some chemical, or the activation of

some receptors, it is possible that those chemicals, at different amounts, or receptors' activation even when a person sleeps normally has some background amount, and that an immunization against those chemicals could reduce the amount of illness the amount of even persons that sleep normally get. it is also possible that germline genetic engineering as well as gene therapy could quantifiably reduce infectious illness of many kinds through causing less of the sleeplessness producing physiochemicals or receptor effects at persons that get normal amounts of sleep.

New genes to optimize and enhance the human germline: I favor publishing all the material I have written, among those materials are notebooks; there is material written in

notebooks as well as online material I have published favoring enhancing as well as optimizing the human germline, **that enhancement as well as optimization can be the result of engineering completely new genes as well as enhancing or optimizing combinations of genes that already exist during 2019AD.**

Raed that during 2019AD pediatricians recommended that babies not sleep with anything in their cribs other than a sheet, perhaps this will improve but until it does, it is possible a flocked sheet with extrasoft flocked patterns on it, like velour macroscopic swirls could be a variation that the baby actually likes feeling the variations of, and where the baby like might moving

**over towards might be a
beneficial enjoyed thing to put on
baby sheets**